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Editorial on Crossing the laboratory borders. Volume I – Health: biosensors and diagnostic tools from the lab to the fab

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The development of new biosensors and biotechnologies observed in recent decades has produced a strong impact in many fields, among which healthcare and wellbeing is certainly one of the most relevant. In particular, the introduction of novel nanomaterials and nanotechnologies has allowed the design of biosensors showing enhanced performance, efficiency, reliability and fast operability, which are aspects especially crucial for point-of-care applications. However, despite the wide range of innovative technologies proposed and the excellent results shown in laboratory and reported in specialized journals, only a very little part of these biosensors crosses the threshold of the laboratory to reach the clinical practice and the marketplace.

Among the possible causes of such a huge gap between research developments and actual commercial products are lack of robustness of the new sensors, high fabrication costs, difficult reproducibility, scalability problems, as well as slow and complicated technology transfer procedures, insufficient interest from companies, or even failure in identifying in time a technology with a great potential. How can this gap be filled in? What can we learn from cases of successful transfer from the lab to the market of biosensor devices?

With this special issue a first collection of research articles on biosensors and biotechnologies has been collected focusing not so much on the novelty of the technology itself –which will have already been presented elsewhere— but rather on the following process of increasing the readiness level of the technology, validating it in the clinical environment, transferring to the industry and, eventually, reaching the market.

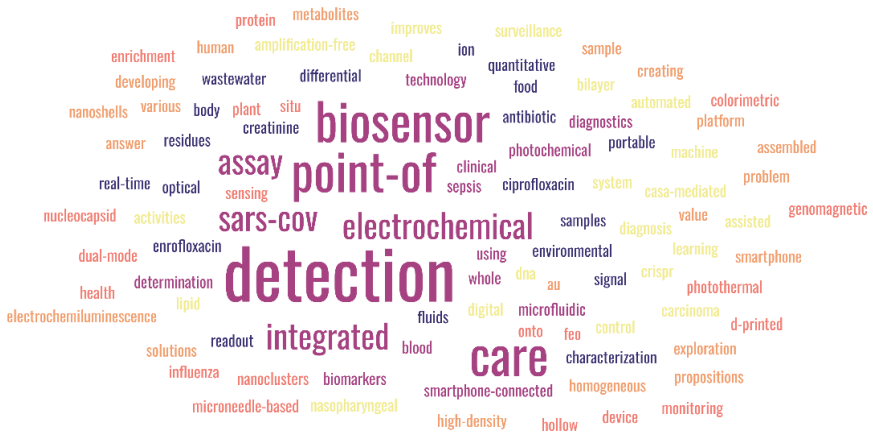


Figure 1. Word cloud of the titles of the publications published in the virtual special issue.

Almeida dos Santos et al. 2024, introduced a genomagnetic assay for the selective capture of viral RNA from SARS-CoV-2 and Influenza A viruses in saliva samples and employing a simple disposable electrochemical device for gene detection and quantification. The assay detects both SARS-CoV-2 and Influenza with LoDs of 5.0 fM and 1 fM, respectively and has been tested on 36 saliva samples with similar responses with respect to RT-PCR.

Bobelyn et al. 2023 has contributed to this special issue by analysing the design process of POC devices intended to reach the market. They did this studying 11 university teams participating in the SensUs contest. The main findings show that teams adopting search patterns involving a 'broader' (i.e., considering a wider range of problems and stakeholders) and a more 'interconnected' (i.e., thematically linking problems with one another) problem-exploration were more successful in creating contest outcomes (biosensing solutions) with greater commercial viability.

Bradley et al. 2023 studied the POC devices available for the sepsis early detection, an issue that requires rapid diagnosis to prevent tragic consequences. Recent advances have been made toward developing a POC test for early sepsis detection that will be more rapid and accurate compared to conventional techniques. Within this context, this review discusses the use of current and novel biomarkers for early sepsis diagnosis using microfluidics devices for POC testing.

Chen et al. 2023 presented the design, fabrication, and feasibility of a compact, low-cost and reliable POC photochemical biosensor connected to a smartphone for the determination of whole blood creatinine by differential optical signal readout. A handheld optical reader was integrated with dual-channel differential optical readout to address endogenous interferences in the enzymatic assay of creatinine. The sensor's high reliability was confirmed through comparison with the laboratory method, with the results of 43 clinical tests consistent with the bulky automatic biochemical analyzer, with its correlation coefficient R2 = 0.9782.

Jiang et al. 2023 focused their efforts on the sensitive and accurate cell-free plasma Epstein-Barr virus (EBV) DNA measurement, essential in the routine diagnosis, monitoring and treatment of Nasopharyngeal Carcinoma (NPC). They developed a CRISPR/Cas12a-mediated amplification-free digital DNA assay, which targets the repetitive sequences of EBV DNA and utilizes the cis-cleavage activity of CRISPR-Cas12a prior to droplet generation. By this mean, more activated Cas12a-crRNA duplexes could be produced for subsequent target detection and counting, thus improving the performance in detecting low EBV DNA load. They demonstrated that it was more robust than conventional qPCR for detecting plasma EBV DNA in a case-control study of 208 participants, especially when the target concentrations were around the diagnostic cut-off value for NPC. More importantly, this assay allowed a more accurate diagnosis of early-stage NPC, with an area under the curve (AUC) of 0.9883 (versus 0.7682 for qPCR). Furthermore, its absolute quantification capability enabled dynamic monitoring of EBV load in NPC patients during initial diagnosis, treatment, and recurrence, thereby potentially improving disease management and prognosis.

Kumar et al. 2023 introduced a 3D Printed ECL imaging system integrated with a Smartphone demonstrating that it advances the traditional ECL to make a portable, affordable, and turnkey point-of-care solution to detect various human metabolites. A universal cross-platform application was introduced for analyzing ECL emitted signals to automate the whole detection process for real-time monitoring and rapid diagnostics. For glucose and lactate detection, the device showed a linear range from 0.1 mM to 1 mM and 0.1 mM–4 mM with a detection limit (LoD) of 0.04 mM and 0.1 mM, and a quantification limit (LoQ) of 0.142 mM and 0.342 mM, respectively. The findings suggested that the developed miniaturized point-of-care ECL platform would be a comprehensive and integrated solution for detecting other human metabolites and have the potential to be used in clinical applications.

Li et al. 2023 developed a polyethylenimine (PEI)-mediated approach for assembling high-density Au nanoshells onto Fe3O4 nanoclusters (MagAushell) as LFIA labels for integrated enrichment and photothermal/colorimetric dual-mode detection of SARS-CoV-2 nucleocapsid protein (N protein). With MagAushell, N protein was first separated and enriched from complex samples, and then loaded to the strip for detection. By observation of the color stripes, qualitative detection was performed with naked eye, and by measuring the temperature change under laser irradiation, quantification was attained free of sophisticated instruments. The photothermal detection limit reached 43.64 pg/mL which was 1000 times lower than colloidal gold strips. Moreover, this method was successfully applied to real samples, showing great application potential in practice.

Enrofloxacin (ENR) and its metabolite Ciprofloxacin (CIP) are both a class of fluoroquinolone antibiotics effective against a broad-spectrum microbial infection. Recent surge in the consumption of CIP and ENR has been linked to increased cases of drug-resistant pathogens. *Mathai et al. 2023* developed a portable device that can detect the presence of CIP and ENR antibiotics in the range of parts per billion (ppb) concentrations accurately. It consists of a polyaniline (PAni) coated U-bent optical fiber with anti-ENR/CIP antibody immobilized on the polymer surface. The sensor relies on the principle of evanescent wave absorbance by antigen-antibody complex. The sensor showed limit of detection (LOD) of 1 ppb with a linear range of operation from 1 ppb to 500 ppb (R2 = 0.96-0.99) in lake water, waste water treatment plant effluent, urine, blood serum, milk and meat samples. The recovery of the sensor ranges from 88% to 120% indicating reasonable accuracy. The sensor has excellent selectivity towards CIP and ENR and showed stability for four weeks indicating its field deployability and robustness. The portable sensor is scalable and contract has been given to an industry partner to mass manufacture the device.

Lipid bilayer systems, which enable single-channel level recordings of ion channel activities against physiological stimuli in vitro, are gaining attention in various research fields. Ogishi et al. 2023 report a lipid bilayer system that integrates real-time characterization of ion channel activities and real-time response based on the characterization result. Unlike conventional batch processing, an ion channel signal is divided into short segments and processed during the recording. After optimizing the system to maintain the same characterization accuracy as conventional operation, Ogishi et al. demonstrated the usability of the system with two applications. One is quantitative control of a robot based on ion channel signals. The velocity of the robot was controlled every second, which was around tens of times faster than the conventional operation, in proportion to the stimulus intensity estimated from changes in ion channel activities. The other is the automation of data collection and characterization of ion channels. By constantly monitoring and maintaining the functionality of a lipid bilayer, our system enabled continuous recording of ion channels over 2 h without human intervention, and the time of manual labour has been reduced from conventional 3 h to 1 min at a minimum.

We wish the readers will enjoy this special issue and find all the publications very useful and inspiring for their future works and efforts in the application of biosensors in real scenarios.

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